In re Application of: Shen-Chen Kuo
Serial No.: 10/050,768
Filed: JANUARY 16, 2002

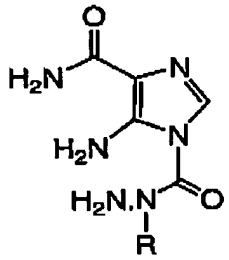
Claim Listing.

This listing of claims will replace all prior versions, and listings, of claims in the application (note that amendments are **highlighted in bold**):

Claim 1. (amended) A process for the preparation of a compound of the formula IA

IA

wherein R is an alkyl group having from 1 to 6 carbon atoms, which comprises reacting a compound of the formula II



II

wherein R is described above, with an oxidation/cyclization agent is **selected from the group consisting of:**

a) periodic acid,

b) iodine/potassium iodate,

In re Application of: Shen-Chen Kuo
Serial No.: 10/050,768
Filed: JANUARY 16, 2002

c) bromine,

d) chlorine; and

e) a reagent that oxidizes NH_2 which is adjacent to the group N-R in the compound formula II, to NZ, where Z represents, Oxygen, (H,Hal), or Hal_2, and wherein Hal is chlorine, bromine or iodine, wherein said oxidation/cyclization reagent is in the presence of an iodide compound, **wherein said iodide compound is quarternary ammonium iodide or inorganic iodide,** in an inert organic solvent, under an inert atmosphere and at a temperature, wherein said iodide is soluble in said inert organic solvent, with the proviso that when said oxidation/cyclization agent is not an iodide, the iodide compound itself is the oxidation/cyclization agent.

Claim 2. (original) The process of claim 1 wherein R is an alkyl group having 1 to 4 carbon atoms.

Claims 3 to 4 (cancelled)

Claim 5. (amended) The process of claim 4 **1** wherein said iodide is selected from the group consisting of Bu_4NI and KI.

Claim 6. (amended) The process of claim 4 **1** wherein said inert organic solvent is selected from the group consisting of:

a) an amide;

b) an acyclic ether;

c) a cyclic ether;

d) an alkyl alkanoate wherein the alkyl group has 1 to 4 carbon atoms and the alkanoate group has 2 to 4 carbon atoms;

e) a halogenated hydrocarbon;

f) toluene; and

(g) mixtures thereof.

In re Application of: Shen-Chen Kuo
Serial No.: 10/050,768
Filed: JANUARY 16, 2002

Claim 7. (previously presented) The process of claim 6 wherein the organic solvent is selected from the group consisting of:

a) DMF;

b) t-butyl-methyl ether;

c) THF;

d) acetonitrile;

e) methylene chloride; and

f) mixtures of the above solvents.

Claim 8. (original) The process of claim 7 wherein the reaction takes place at a temperature of about (-)20°C to about (+) 70°C and under a nitrogen atmosphere.

Claim 9. (previously presented) The process of claim 6 wherein:

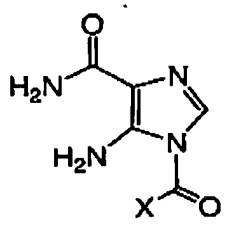
a) the organic solvent is a 50/50 mixture of THF/CH_3CN;

b) the oxidation/cyclization agent is H_5IO_6;

c) the iodide is Bu_4NI and

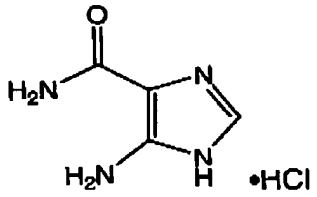
d) the reaction takes place at a temperature of about 0°C to about (+)60°C.

Claim 10. (previously presented) A process for preparing a compound of the formula III:



III

which comprises reacting a compound of the formula 4:



4

with a compound of the formula X-CO-Y in the presence of an acid binding agent, wherein each of X and Y is the same or different leaving group, with the proviso that X is not 4-nitrophenyloxy group, to yield a compound of the formula III, wherein X of said compound X-CO-Y is selected from the group consisting of

a) phenyloxy;

b) 2-naphthyloxy and

c) substituted phenyloxy, and wherein Y of said compound X-CO-Y is selected from:

a) chlorine,

b) bromine, or

c) iodine;

and wherein the substituents on said substituted phenyloxy group are selected from the group consisting of:

a) 2-nitro;

b) pentafluoro;

c) chlorine;

d) bromine;

e) iodine, and

f) combinations of the above.

Claim 11. (canceled)

In re Application of: Shen-Chen Kuo
Serial No.: 10/050,768
Filed: JANUARY 16, 2002

Claim 12. (canceled)

Claim 13. (original) The process of claim 10 wherein said reaction of the compound of the formula 4 with a compound of the formula X-CO-Y is performed in the presence of an acid binding agent, in an inert organic solvent, under an inert atmosphere and at a temperature of about (-) 20°C to about (+) 50°C.

Claim 14. (original) The process of claim 13 wherein said acid binding agent is a tertiary amine.

Claim 15. (previously presented) The process of claim 13 wherein the organic solvent is selected from the group consisting of

a) an amide;

b) an acyclic ether;

c) a cyclic ether;

d) an alkyl alkanoate wherein the alkyl group has 1 to 4 carbon atoms and the alkanoate group has 2 to 4 carbon atoms;

e) a halogenated hydrocarbon, and

f) mixtures thereof.

In re Application of: Shen-Chen Kuo
Serial No.: 10/050,768
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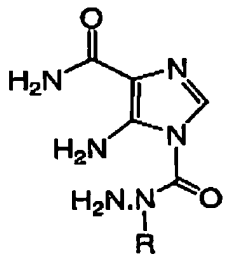
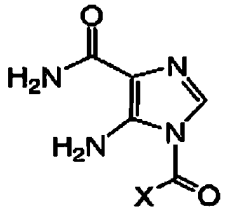
Claim 16. (previously presented) A process for the preparation of a compound of the formula II:



II

wherein R is an alkyl group having from 1 to 6 carbon atoms, comprising, reacting a compound of the formula III:



III

wherein X is a leaving group with an alkylhydrazine having from 1 to 6 carbon atoms.

Claim 17. (original) The process of claim 16 wherein said alkylhydrazine is R-NH-NH_2, wherein R is an alkyl group having 1 to 4 carbon atoms.

Claim 18. (original) The process of claim 16 wherein the reaction takes place in an inert organic solvent selected from the group consisting of:

a) a non-nucleophilic amine and

b) an ether; and

c) mixtures thereof.

Claim 19. (original) The process of claim 16 wherein X is selected from the group consisting of:

a) phenyloxy;

b) 2-naphthyloxy and

c) substituted phenyloxy, wherein the substituents are electron withdrawing.

Claim 20. (original) The process of claim 19 wherein said substituents are selected from the group consisting of:

a) 2-nitro;

b) 4-nitro;

c) pentafluoro;

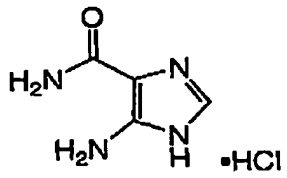
d) chlorine and

e) bromine.

Claim 21. (previously presented) The process of claim 17 wherein said compound of formula II is a 1-alkyl derivative of 5-amino-4-(aminocarbonyl)-1H-imidazole-1-carboxylic acid hydrazide wherein the alkyl group contains 1 to 6 carbon atoms.

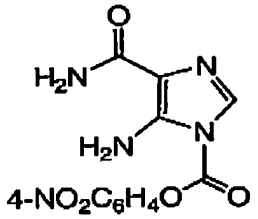
Claim 22. (previously presented) The process of claim 21 wherein said compound of formula II is 5-amino-4-(aminocarbonyl)-1H-imidazole-1-carboxylic acid 1-methylhydrazide.

Claim 23. (original) The process of claim 14 wherein compound 4:



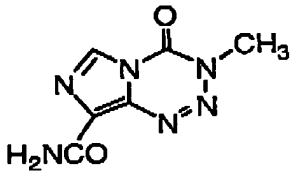
4

is reacted with 4-nitrophenyl chloroformate, in the presence of triethyl amine, said reaction taking place in methylene chloride solvent, under a nitrogen atmosphere and at a temperature of about (-)20°C to about (+) 50°C to yield compound (3):



(3)

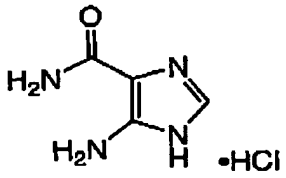
Claim 24. (previously presented) A process for preparing temozolomide (1):



(1)

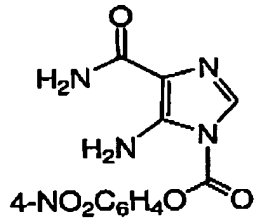
comprising:

a) reacting compound 4:



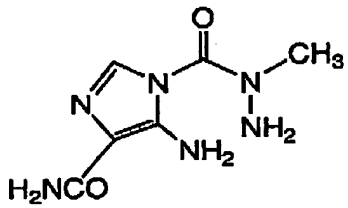
(4)

with 4-nitrophenyl chloroformate in the presence of triethylamine in CH_2Cl_2 under a nitrogen atmosphere at about 25°C to obtain compound (3):



3 ;

b) reacting compound (3) with methylhydrazine in DMF at about 0°C to obtain compound (2):



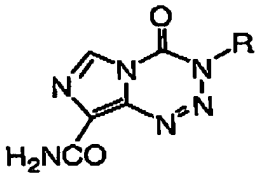
(2) , and

c) reacting compound (2) with Bu_4NI in a 50/50 mixture of THF/CH_3CN, at a temperature of about (+) 60°C for a time of about 0 to about 60 minutes, followed by the cooling of the reaction mixture to about (+) 25°C and the addition of H_5IO_6 and stirring for about 10 to about 60 minutes to obtain temozolomide (1).

Claims 25-28. (cancelled)

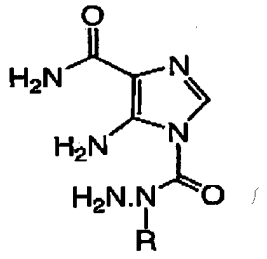
In re Application of: Shen-Chen Kuo
Serial No.: 10/050,768
Filed: JANUARY 16, 2002

Claim 29. (New) A process for the preparation of a compound of the formula IA



IA

wherein R is an alkyl group having from 1 to 6 carbon atoms, which comprises reacting a compound of the formula II



II

wherein R is described above, with an oxidation/cyclization agent, where said oxidation/cyclization agent is H_5IO_6, in the presence of an iodide compound, where said iodide compound is Bu_4NI, in an inert organic solvent, under an inert atmosphere and at a temperature, wherein said iodide is soluble in said inert organic solvent, with the proviso that when said oxidation/cyclization agent is not an iodide, the iodide compound itself is the oxidation/cyclization agent.